

CLAIMS

1. High-performance dispensing system of micro-droplets, comprising a substrate (2) covered by a membrane (3) and means (65, 70)

5 for deforming the membrane perpendicularly to each cavity (10) formed in the substrate (2), characterised in that the cavities, etched in a material composing the substrate, appear in the shape of wells crossing the substrate with a continuous lateral wall (11) of axial symmetry, and in that each well opens on the upper surface and the lower surface of the substrate

10 as respectively a feeding opening (12) and a duct (14) opened as an ejection nozzle (13), the feeding opening presenting an opening higher than the nozzle (13) of the duct, and the duct presenting a shape ratio between 1 to 20.

15 2. Dispensing system of micro-droplets according to claim 1, wherein the well density reaches $10\,000/\text{cm}^2$, with a flow of at least one million droplets per second.

3. Dispensing system of micro-droplets according to claim 1, wherein the wells are configured in matrix form, circular concentric form, in spiral, or according to a combination of these configurations.

4. Dispensing system of micro-droplets according to any one 20 of the previous claims, wherein the membrane or the substrate has a multi-layered structure that integrates the micro-ducts tri-dimensionally in different layers, the micro-ducts then being coupled to the wells by connections perpendicular to the upper openings of the wells.

5. Dispensing system of micro-droplets according to any one 25 of the previous claims, wherein the whole of the means for deforming is managed by a control unit programmable through a multiplexing network to trigger simultaneously or successively the suction or the ejection of identical or different reagents through the wells, by blocks of pre-selected wells or by certain pre-selected wells.

30 6. Dispensing system of micro-droplets according to any one of the previous claims, wherein the material of the substrate or of the membrane is chosen among semiconducting materials, polysilicon, glass, silicon nitrides, ceramics, thermoplastic materials, elastomers, thick photosensitive resins, and electro-formed or electro-eroded metals.

35 7. Dispensing system of micro-droplets according to claim 5 or 6, wherein the etching of the substrate or of the membrane is chosen among

chemical etching, RIE, D-RIE, photolithography, etching by electroerosion or electroforming(6), moulding and polymerisation, laser cutting, ultrasounds, or the projection of abrasives.

8. Dispensing system of micro-droplets according to claim 7,
5 wherein the membrane is etched to create a network of micro-ducts to feed the wells, said micro-ducts being coupled at the tip to at least one reagent feeding reservoir.

9. Dispensing system of micro-droplets according to claim 1,
10 wherein the means for locally deforming (65, 70) the membrane (3) are composed of electromagnetic, piezoelectric, magnetostrictive, electrostatic actuators or by electro-evaporation.

10. Dispensing system of micro-droplets according to claim 1,
wherein the deformation forces on the membrane are generated by starting a resonance of the membrane (3) or by vibration of the tip of the ducts (14).

15 11. Dispensing system of micro-droplets according to claim 1,
wherein the wells in each line of a matrix configuration are fed by the same reservoir (4) through a micro-duct (20) formed in the membrane parallel to the line of wells (10) and coupled laterally to the line or orthogonally to the plane of the substrate (2), the reservoirs being etched in the membrane or positioned at 20 a distance and linked to the micro-ducts by flexible connections.

12. Dispensing system of micro-droplets according to claim 1,
25 wherein the dispensing head (1) has a number of lines equal to a multiple of four, in order to proceed to the synthesis of probes of DNA from the four mononucleotides (A, C, T, G) for the preparation of bio-chips, and wherein the wells in each line are fed by the same reservoir through a micro-duct (32) formed in the membrane (3) parallel to the lines, the reservoirs being etched in the membrane or positioned at a distance and linked to the micro-ducts by flexible connections (7).

30 13. Dispensing cartridge comprising at least a dispensing system according to any one of the previous claims, pre-filled with reactants (51), and with titration plates (81) that can show micro-bowls (80) formed by micro-electronic type etching, by manufacturing, by moulding, and by thermoforming.

35 14. Dispensing kit comprising at least a dispensing system according to any one of claims 1 to 12, equipped with at least one aspiration

pump (8), and at least one titration plate (81), which can be pre-filled with reagents.

15. Cartridge according to claim 13 or kit according to claim 14, wherein the titration plate shows micro-bowls equipped with polarised electrodes, the cell reactivity test being optical or electrical.

16. Titration plate according to claim 15, wherein a potential difference is applied between said electrodes in order to generate a polarisation in the cell and favour the therapeutical effect on the cells.

17. Application of the cartridge according to claim 13 or of the kit according to claim 14 to the preparation of bio-chips, by synthesis in situ or deposit of pre-synthesised oligonucleotides, to the screening of biological, chemical molecules, or on cells, to the preparation of drugs or to pharmaceutical tests or of immunological, biochemical or genetic screening.

18. Application of the dispensing system according to any one of the claims 1 to 10, to the percutaneous administration of drugs by iontophoresis consisting of an application system of a difference of potential suitable on a piezoelectric cell (70) for the administration of a calibrated quantity of at least one drug contained or formed in at least one well.

19. Application to the screening of test cells in pharmacology of a dispensing system according to any one of the claims 1 to 12, wherein drugs are deposited on the cells contained in the micro-bowls (80) of a titration plate (81), equipped with polarised electrodes, the cell reactivity test being optical or electrical.

20. Application according to the previous claim, where a potential difference of adapted value is applied between said electrodes in order to generate a polarisation in the cells and thus favour the therapeutic effect on the cells.

21. Application of the dispensing system according to any one of the claim 1 to 14, to the selective filtration by fixation on the walls of the wells of a dispensing head for identical or different bio-cells or for the biochemical compounds by well or by block of wells.

22. Application of the dispensing system according to the previous claim, where the dispensing head is integrated to the tip of a syringe.

23. Application of the dispensing system according to any one of the claims 1 to 14, to the parallel or sequential feeding of the columns of mass spectrometer or of chromatographs.



DESCRIPTIVE ABSTRACT

HIGH-PERFORMANCE PARALLEL AND SELECTIVE DISPENSING SYSTEM OF MICRO-DROPLETS, TRANSPORTABLE CARTRIDGE AS WELL AS INSTALLATION DISPENSING KIT, AND APPLICATIONS OF SUCH A SYSTEM

This invention aims at allowing a consistent increase in the output of selective dispensing of micro-droplets, at making a spatial, targeted selectivity by distributing a predetermined reagent on the predetermined site, and at creating a multifunctional system, easy to adjust.

An example of dispensing system according to this invention consists of a substrate (2) covered by a membrane (3) and of means for deforming (65) the membrane at the right of each cavity formed in the substrate, and where the cavities, etched in a material constituting the substrate (2) in a matrix shape, appear in the shape of wells (10) crossing the substrate with lateral, continuous walls (11) of axial symmetry; each well opening on the upper surface and the lower surface of the substrate with respectively a feeding opening (12) and an ejection duct (14), the feeding opening showing an opening consistently higher than the opening (13) of the duct.

Application to the manufacturing of cartridges and of miniaturised kits in biochemistry and pharmacy, or also in cosmetics, in analytical instrumentation, in printing by inkjet or in the automobile electronics.

FIGURE 13a.